Synthetic Organic Chemicals

PUBLISHED BY THE
EASTMAN KODAK COMPANY, ROCHESTER, NEW YORK

VOL. III | PUBLISHED APRIL, 1930 | NO. 4

Thionyl Chloride in Organic Synthesis

THE value of thionyl chloride in the preparation of organic compounds has long been known although for a time the high cost restricted its use. New catalytic methods for making it from carbon monoxide, chlorine, and sulfur dioxide, developed in recent years, have lowered its cost substantially. As can be seen from its formula $SOCl_2$ it may be considered as an acid chloride of sulfurous acid in the same way that $POCl_3$ is an acid chloride of phosphoric acid. Consequently it has many of the reactions common to phosphorus oxychloride. When pure it is a colorless liquid with a high refractive index. It has a sharp, penetrating odor and fumes when exposed to moist air. The boiling point is 78.8°C at atmospheric pressure. The commercial product usually has a light yellow color which can be removed by adding a small amount (3%) of linseed oil and redistilling.

Probably the most common use of thionyl chloride is to replace phosphorus trichloride or pentachloride in the preparation of acid chlorides from the corresponding acids, according to the following reaction:

$$RCOOH + SOCl_2 \rightarrow RCOCl + SO_2 + HCl$$

A typical example of this reaction is shown in the preparation of acetylmandelyl chloride described by Thayer in Vol. 4 of ORGANIC SYNTHESES. The acetylmandelic acid is refluxed for four hours with an excess of thionyl chloride during which time sulfur dioxide and hydrogen chloride are evolved. Owing to its low boiling point, any remaining thionyl chloride can be distilled off readily, leaving behind the crude acid chloride. On vacuum distillation this product yields 80% of the theoretical amount of acetylmandelyl chloride. In addition to the improved yield, the troublesome handling of solid phosphorus pentachloride is avoided. Furthermore, since the side-products are gases and the reagent itself a low boiling liquid, there is no difficulty whatever in isolating the final product. The preparation just described is typical, the reaction starting smoothly at room temperature and requiring warming only on a steam bath for completion.

In contrast to phosphorus pentachloride, thionyl chloride seldom reacts with an aldehyde, ketone, or ethoxy group. This permits its use with many acids of complicated structure where one of these radicals is located near the carboxyl group. For instance, the acid chloride of methyl malonic acid is produced in good yield from potassium methyl malonate with a slight excess of thionyl chloride. Neither is the OH group of salicylic acid attacked when the acid chloride is made by this method.

In the case of amino-acids, the reaction with thionyl chloride can be confined to the carboxyl group by replacing one of the amino hydrogen atoms with a carbethoxy group. Carbethoxyglycyl-

glycine is easily converted into the acid chloride without disturbing side reactions. A few acids, such as oxalic, parahydroxybenzoic, and trichloroacetic, are exceptions and do not yield acid chlorides by this method. In other cases, instead of the acid chloride, the anhydride is formed as shown by the equation:

$$2\ RCOOH + SOCl_2 \rightarrow (RCO)_2O + SO_2 + 2HCl$$

Acetylsalicylic, phthalic, and maleic anhydrides can be obtained in this way. A convenient method of preparing o-sulfobenzoic anhydride for the synthesis of some of the Clark and Lubs indicators is to treat acid ammonium o-sulfobenzoate with thionyl chloride in benzene solution.

This dehydrating action of thionyl chloride also assists in the preparation of many esters. For this work, the reaction is usually carried out at a low temperature in the presence of a small amount of pyridine. Isoeugenyl benzoate and p-nitrophenyl anisate are readily formed in this manner by treating the acids with isoeugenol and p-nitrophenol. When amines are used in place of phenols, the corresponding anilides are obtained almost quantitatively. The elements of water are also removed from certain acid amides forming the nitriles, m-nitrobenzamide condensing easily to n-nitrobenzonitrile. In all of these cases, the ease with which the by-products are removed is the striking factor.

A large excess of thionyl chloride in the presence of pyridine reacts with alcohols replacing the hydroxyl group by chlorine in a manner analagous to its action on acids. However, if only the theoretical amount of thionyl chloride is used, the sulfite is formed, the reaction proceeding as follows:

$$2\ ROH + SOCl_2 \rightarrow (RO)_2SO + 2HCl$$

Thus, starting with cholesterol, quantitative yields of cholesteryl chloride or bis-cholesteryl sulfite may be obtained simply by regulating the amounts of thionyl chloride and pyridine. This reagent lends itself also to the introduction of other sulfur groups. Benzene and toluene in the presence of aluminum chloride react to form the sulfoxides, while a number of the other aromatic compounds form sulfides directly.

There are many cases where this versatile compound acts as a catalyst, apparently not entering the reaction itself. For instance, in the Friedel-Craft ketone synthesis, pyridine and quinoline will not condense with either acetyl or benzoyl chloride when aluminum chloride alone is used. If a trace of thionyl chloride is added to the reaction mixture, the ketones are readily formed. When the benzoyl chloride is prepared through the use of thionyl chloride, a trace of the latter compound usually remains so that further addition is unnecessary. There are also a number of other reactions not so generally applicable as the ones mentioned above but which, nevertheless, help to round out its use as a valuable reagent for the organic laboratory.

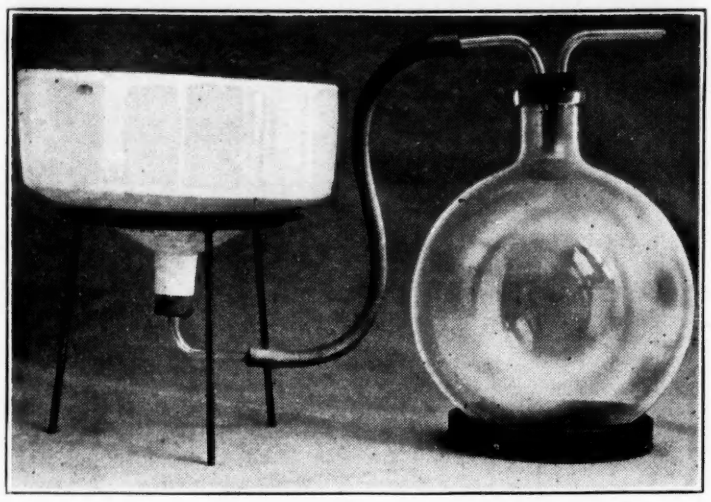
New Eastman Organic Chemicals

A new catalog, List No. 21 of Eastman Organic Chemicals containing over 2,600 items, was issued in January, 1930. During the last three months the following chemicals have been added to the list given therein:

Anisyl Alcohol
*Benzyl Phthalate
Boric Acid (Practical)
*n-Butyl Phthalic Acid
*Ethyl Ethylacetoacetate
Furacrilic Acid (Practical)
Furfural Acetone (Practical)
*Guaiacol Acetate
*Hexamethylenetetramine Alliodide
Mucic Acid (Practical)
Zinc Ethyl

**Made or purified in the Kodak Research Laboratories.*

Novel Filtration Aids



Anyone who has used a large Büchner funnel is aware of the instability of the usual top-heavy set-up. The one shown in the photograph has the advantage of stability and convenience. The stem of the funnel is cut off and a rubber stopper carrying a glass tube is inserted. The outer end of the glass tube is connected by rubber pressure tubing to another glass tube which enters a flask through a two-hole rubber stopper. A glass tube passing through the second hole is connected, by pressure tubing, to the filter pump.

The funnel is supported on a large tripod such as those commonly found in the equipment of chemical laboratories. The apparatus has great rigidity and a high factor of safety since the possibility of the set-up tipping over has been reduced to a minimum, and comparatively small and more rugged receivers can be employed, thus greatly reducing the chance of collapse at low pressures.

Another method of filtering which has proved valuable under certain conditions consists in lowering the funnel into the suspension to be filtered, instead of pouring the suspension into the funnel as is usually done. The Büchner funnel is cut and connected as in the above procedure except that the rubber tube connecting the funnel with the receiver must be somewhat longer. The material to be filtered is placed in a crock and after attaching a moist filter paper to the funnel by mild suction it is immersed in the liquid and the suction increased. This procedure is especially helpful in removing excess liquid from solids which have partly settled out and which will subsequently be separated by centrifuging or "wringing."

The physical character of the material being filtered sometimes makes changes in the filtering medium itself desirable. Scrim, "factory," canvas, or felt often work better than filter paper. In many cases it has been found advantageous to stretch the filtering cloth over the funnel and fasten it at the stem. Such an arrangement can be used with or without a paper or felt over the plate of the funnel. Sometimes when cloth is used over the outside of the funnel, it is advisable to support it by packing the funnel with cotton fibres, glass wool, or similar material.

Where bulky, fibrous materials are being filtered, suction applied in the usual way is valueless unless a layer of the liquid being removed remains on the filter. Without this layer, air is drawn past the particles on the funnel and the only removal of liquid is accomplished by evaporation. To obtain the advantage of atmospheric pressure for such filtrations it is only necessary to cover the funnel with a piece of dental rubber dam somewhat larger than the funnel. The suction forces the rubber down onto the product, thus pressing out much of the residual liquid. The use of the rubber dam is desirable when working with textile fibres or with materials which are easily oxidized in the air, and it has been found that a thickness of about 1.125 mm. (0.045 inch) is quite satisfactory.

Heavy Organic Liquids

The problems of mineral separation require a number of liquids of different specific gravities by means of which the lighter minerals are floated away from the heavier ones which sink. The specific gravity range for the more common minerals varies from 2.6 for feldspar to 8.2 for cinnabar. Very few of the thousands of organic compounds have high enough densities to be of use in this work. More than ordinary interest is therefore attached to the exceptions which have the desired requirements.

Tetrabromoethane, with a specific gravity of 2.95, is an organic chemical which is used very widely for this purpose. By diluting this liquid with carbon tetrachloride, liquids having any specific gravity between 1.60 and 2.95 may be obtained. For instance, a mixture of 93 parts by volume of tetrabromoethane with 7 parts of carbon tetrachloride will give a liquid with a specific gravity of 2.8. Since quartz (s.g. 2.6) and calcite (s.g. 2.7) constitute the gangue of many ores, this mixture of liquids is heavy enough to float the gangue from the other minerals present.

An aqueous solution of thallium formate is used for the range of 2.95 to 3.5. The solubility of thallium formate in water at ordinary temperatures is not high enough to give a specific gravity much above 3.4. The solubility increases rapidly with temperature, however, so that at 42° C., a 90% solution has a specific gravity of 3.7, while at 60° the 95% solution has a density of 4.2.

The specific gravity of the double salt, thallium formate-malonate, is greater than that of either alone. With proper adjustment of concentration and temperature, a liquid with the extremely rare specific gravity of 4.9 is obtained.

Technical paper No. 381 of the Bureau of Mines discusses in detail the properties of these liquids.

Eastman Organic Chemicals as Analytical Reagents

XIV

REAGENTS FOR ZINC

(Continued)

DIPHENYLAMINE

Cone and Cady, J.A.C.S. *49*, 2214 (1927)

A qualitative reagent for zinc consists of one gram of diphenylamine in 100 cc. of glacial acetic acid. The alkaline filtrate containing the aluminum group is treated with hydrochloric acid and ammonium chloride, after which the aluminum is precipitated with ammonium hydroxide. After filtering off the aluminum hydroxide, the filtrate is divided into two parts, one of which may be tested for chromium. To the part to be tested for zinc are added 5 drops of the above reagent and 5 cc. of 0.5% potassium ferricyanide. The immediate appearance of a green, dark brown or purple-black turbidity shows the presence of zinc which can be estimated by the depth of color produced.

PYRIDINE

Spacu and Dick, Z. Anal. Chem. *73*, 356 (1928)

Addition of pyridine and ammonium thiocyanate to neutral solutions of zinc salts gives quantitative precipitation of a compound containing 19.25% zinc. The precipitate is washed successively with four different solutions (1) 3 gm. ammonium thiocyanate and 5 cc. pyridine per liter of water. (2) 13 cc. 95% alcohol, 85.5 cc. water, 1.5 cc. pyridine and 0.10 gm. ammonium thiocyanate. (3) 10 cc. absolute alcohol containing 1 cc. pyridine. (4) 15 cc. ether containing 2 drops of pyridine. Under different conditions, the same reagents may be used to precipitate other metals.